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Pain Interventions For Organ Transplant Patients Undergoing Incisional Hernia Repair – Is Epidural or Transversus Abdominus Plane Block A Better Option?

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Running Head: analgesia for post-transplant hernia repair

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Clin Transplant

Abstract

Post-operative pain management in transplant recipients undergoing incisional herniorraphy is challenging. Historically limited to intravenous or oral opioids, alternatives including transversus abdominus plane (TAP) block catheters and thoracic epidural catheters have been introduced . The aim of this study was to determine whether TAP catheters and thoracic epidural analgesia significantly impacted on postoperative pain and opioid usage in transplant recipients undergoing incisional hernia repair. **Methods:** This single center retrospective study included 154 patients undergoing incisional hernia repair from January 2011 to June 2015. Of these, 56 received epidurals, 51 received TAP catheters, and 47 received no intervention. **Results:** demographic profiles were comparable among the three groups including type of previous transplant and type of hernia surgery. Thoracic epidural analgesia was associated with lower median, mean, and maximum pain scores ($P<0.001$) and less opioid requirement ($P<0.001$). There was no difference in pain scores and opioid usage among the TAP catheter and no intervention groups. There was no difference in time to first flatus or first bowel movement, length of hospital stay, individual opioid-related side effects, and adverse reactions among the 3 groups. **Conclusion:** This study supports the use of thoracic epidural analgesia in patients undergoing hernia repair after transplant surgery.

Key words: Transplantation surgery, incisional hernia, Transversus abdominus plane block, epidural analgesia

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Introduction

An abdominal organ transplant operation typically involves a long incision, followed by high dose induction immunosuppression; both of which are considered risk factors for an incisional hernia.[1] Unsurprisingly, herniorrhaphy is commonly required after transplantation, with some reporting an incidence as high as 35% following liver and pancreas transplants (kidney transplant incisions, being lateral, have a much lower incidence).[1] One challenge of incisional hernia repairs is intense postoperative pain.[1,2,3] Parenteral pain control is the cornerstone of pain management in those cases, but it can be associated with ileus, respiratory depression, pneumonia, and aspiration.[3,4,5,6] Increased opioid use has been associated with an increase in length of ICU and hospital stay.[7] On the other hand, inadequate pain control can lead to pneumonia, delayed wound healing, and increased length of stay.[8,9] In transplant patients, these problems are magnified by immunosuppression, making the issue of adequate pain control key in avoiding complications in this patient population.[1]

To address these challenges, we began using continuous TAP (transversus abdominis plane) blocks for post-herniorraphy analgesia in 2013. However, even in patients undergoing a laparoscopic hernia repair with small incisions, we noticed that analgesia with continuous TAP blocks was not meeting the needs of our patients as well as we had hoped. This was most likely due to the underlying mesh size and the area of mesh fixation, which are much larger than the incision size. Also, liver transplant hernias, located in the upper abdomen, are poorly covered with a TAP block. We therefore transitioned to offering thoracic epidural analgesia to this group of patients.

Epidural analgesia for post-operative pain control has been shown to decrease total opioid consumption.[10], [11],[12],[13] However, epidural use is potentially problematic in immunosuppressed patients, due to the theoretical risk of meningitis, epidural abscess, or other infectious complications.[14] Overall, infectious complications associated with regional anesthesia are very rare events.[15] Some studies report 1 infectious complication (nervous system infection, epidural abscess, etc) for every 40,000 regional nerve blocks. Others report 1 infectious event per 100,000 blocks .[16] Nevertheless, the possibility exists that the risk of these rare, but potentially devastating, infectious complications could be increased in an immunosuppressed patient population. Therefore, in setting up an epidural protocol for immunosuppressed patients, we considered avoidable factors that might increase infectious complications in immunosuppressed patients.

First, in those rare cases of infection following regional anesthesia, duration of epidural placement appears to play a role.[17] Therefore we usually limit epidural placement in immunosuppressed patients to four days.

Second, the immunosuppression following transplantation is most intense in the early post-transplant period. Therefore we try to avoid hernia repair in the first 6 months post-transplant. After that period, the immunosuppression is much less intense.

Third, the type of immunosuppression may affect the risk of complications. The infectious complications reported after epidural catheter placements are mainly bacterial. However, not all immunosuppression regimens are equally prone to bacterial infections, which are mainly the hallmark of corticosteroid based immunosuppression. In contrast, steroid-free immunosuppression tends to be associated with viral infections or other non-bacterial infections that would not be typical of an epidural catheter-associated infection. We reasoned that thoracic epidural catheters in transplant recipients on steroid-free immunosuppression have a reasonable risk-benefit profile. Of note, our institution's long-term immunosuppression regimen is usually steroid-free. Another concern with immunosuppressive agent is wound healing. Our institution only uses rapamycin routinely for kidney/pancreas transplant patients. Liver and kidney transplant recipients do not receive long term rapamycin. For patients on rapamycin, we routinely convert the agent to mycophenolate prior to coming to the OR, due to concern with wound healing.

Finally, in order to minimize the risk of infectious complications, we place all of our epidural catheters in the operating room under sterile conditions. The anesthesiologists scrub and wear sterile gowns and gloves for all epidural catheter placements.

Given the paucity of literature published to date on use of epidural analgesia in immunosuppressed patients, the primary aim of this study was to investigate the difference in postoperative pain intensity and opioid usage between organ transplant patients who underwent incisional hernia repair with epidural analgesia compared to those who received continuous TAP blocks and those who received no regional analgesia. Secondary aims of this study were to examine differences in time to first flatus and bowel movement, and opioid-related side effects (nausea, vomiting, respiratory depression, pneumonia, and aspiration) between patients who received epidural analgesia, continuous TAP blocks, or no regional analgesic intervention.

Methods

Indiana University Hospital is a large academic medical center where 40-50 herniorraphy operations are performed per year in patients who have undergone prior organ transplantation. Following review and approval by the Indiana University institutional review board, we performed a retrospective chart review. All regional anesthesia procedures at our institution were done under supervision of an Acute Pain Service attending. All TAP catheters are done under ultrasound (US) visualization. After identifying the Transversus Abdominis Plane on US, the anesthesiologists will inject 0.2% ropivacaine into each TAP space. All patients will then have an elastomeric pain relief ball (OnQ) attached to the TAP catheter in PACU to provide continuous infusion. All thoracic epidurals are done in the operating room under sterile condition. We scrubbed, gowned, and gloved for all epidurals due to the immunosuppressive state on all these patients. The epidurals are placed between T8-T10 level. Standard epidural mix in our institution is bupivacaine 0.1%/hydromorphone 0.05mg/ml. All epidural infusions are started in PACU to provide continuous infusion. As far as pain scores and opioid usage, pain scores were evaluated every 6 hours in our institution using Visual Analog Scale (VAS). All recorded pain scores were collected and analyzed for daily mean, median, and maximum score. Daily opioid usage were also recorded and all opioid recorded were converted to IV morphine equivalent each day.

Study Population

All solid organ transplant patients undergoing incisional hernia repair between January 1, 2011 and June 30, 2015 at Indiana University Hospital were identified using billing data and reviewed through medical records or Cerner/Care web according to inclusion and exclusion criteria. All post-transplant patients who underwent elective incisional hernia repair under general anesthesia were included. These patients all receive either a "Mercedes" (liver) or a midline (pancreas) incisions during their initial surgery. Patients with perioperative bowel or organ injury, recurrent ventral hernias, or incarcerated hernias were excluded. Further exclusion criteria included current daily opioid use, contraindications to morphine or hydromorphone, diagnosis of "chronic pain syndrome," and a known history of substance abuse. Patients younger than 18 years of age were excluded. Overall, we collected data on 154 transplant recipients undergoing incisional hernia repair including 56 patients who had received epidural analgesia, 51 patients who had received continuous TAP blocks, and 47 patients who had received no intervention.

Data from the postoperative period was obtained from patient charts, anesthesia records, ICU notes, and the transplant registry. Demographic data was collected from patient electronic medical records. The data obtained included pain intensity scores from day 1 to day of discharge, opioid usage, time to first flatus, time to first bowel movement, length of hospital stay, and occurrence of opioid-related side effects including nausea, vomiting, respiratory depression, pneumonia, and aspiration.

Statistical Analysis

Demographic comparisons between the three groups were performed using a two-sample t-test for continuous variables and a chi-square test for categorical variables. The mean and standard error were calculated for all of the continuous endpoints (e.g. pain scores by day and across all days, time to first flatus, time to first bowel movement, length of stay) and frequency with percentage for categorical endpoints (e.g. opioid use, each type of opioid-related side effect).

A linear mixed model was performed to analyze pain scores over longitudinal data (7 days per patient). Median, mean, and maximum pain scores from potentially 12 pain scores per patient per day were first calculated and then used as outcomes.

A linear regression model was used for analyzing the three cross-sectional outcomes, time to flatus, time to bowel movement, and length of hospital stay.

Opioid-related side effect frequency was calculated based on the presence of opioid-related side effects on any day. A logistic regression model was performed to investigate possible influential factors for the occurrence of opioid-related side effects.

Patients' age at surgery, BMI, type of transplant, duration of surgery, and amount of blood loss were included in all the statistical models. In addition, time effect –variable 'countday', was included in the mixed model for pain score analysis. For all calculations, p-values less than 0.05 were considered significant. All calculations and data analysis were performed using SAS statistical software version 9.2 (SAS Institute Inc., Cary, NC).

Results

The patient demographics (Table 1) show that the patients in the 3 study groups (epidural, continuous TAP block, or no analgesic intervention) were similar with respect to age, gender, and BMI. Interestingly, patients who received epidural analgesia had significantly less intra-operative blood loss than those who did not have an epidural ($P<0.001$; Table 1). This is likely due to selection bias since epidural catheter placement is contraindicated in patients with coagulopathies. Patients rated their pain scores using a numerical rating scale. Patients who received epidural analgesia reported significantly lower median, mean, and maximum pain scores than those who did not have an epidural ($P<0.001$). Patients with epidural analgesia also used significantly less opioids ($P<0.001$). Tables 2, 3, and 4 show the pain scores and opioid usage comparisons for the first, second, and third post-operative days, respectively. Patients who received epidural analgesia reported significantly lower median, mean, and maximum pain scores on each individual day ($P<0.05$; Tables 2, 3, 4). Patients who received epidural analgesia used significantly less opioids on post-operative day 1 ($p<0.001$; Table 2) and day 2 ($p=0.014$; Table 3). The difference in opioid usage between patients who received epidural analgesia and those who did not were not as significant by day 3 ($p=0.084$; Table 4), but continued the

trend of lower opioid consumption by patients who received epidural analgesia. Data from later days were not analyzed as patients typically had their epidural or TAP block catheters removed on day 3.

Patients in the epidural group did not show an increased in incidence of side effects when compared with the non-epidural group (Table 5). The time to first flatus, time to first BM, and hospital length of stay was not statistically significant among the groups as well (Table 6).

Discussion

This study was a retrospective analysis of pain control methods for organ transplant recipients who are undergoing hernia repair. Our primary endpoints were pain scores and post-operative opioid consumption. The patients who received epidural analgesia had a significant reduction of median and mean pain scores as well as opioid consumption compared to the patients in the other two groups. This shows that epidural analgesia is superior to either continuous TAP blocks or pain control without a regional analgesic intervention.

With regard to our secondary endpoints, we hypothesized that an analgesic intervention which reduced oral and intravenous opioid consumption would reduce the incidence of side effects and complications associated with opioid analgesia. We were interested to see that this hypothesis was not confirmed. There was no significant difference in time to first flatus, time to first bowel movement, length of hospital stay, individual opioid-related side effects, or adverse reactions between those who received epidural analgesia and those who did not. Interestingly, we see a slightly higher hospital length of stay (though not statistically significant) in our epidural populations. This is likely due to selection bias since patients with very big complex hernias are not candidate for TAP catheters and will only be offered epidurals for their complex hernia repairs.

Addressing the safety of epidural analgesia in this patient population, we noted that no major opioid-related side effects were reported in any of the patients in the epidural group. No infectious complications related to the analgesic intervention occurred in any of these immunosuppressed patients.

The strength of this retrospective study is that all hernia repairs are done by a single transplant surgeon here in our institution, hence there is no difference in surgical technique or perioperative management amongst the groups. Mesh size was based on overlap onto healthy tissues of at least 4cm all directions. In addition, the entire incision was assessed for possible weakness or incipient hernia ("Swiss cheese hernia"). In most cases, the entire incision was reinforced with mesh. Since transplant incisions are large regardless of whether it was a liver transplant or pancreas transplant, this usually meant using the largest piece of mesh available, tailored to the shape of the hernia defect and the 4 cm overlap all edges. Most common mesh sizes use for our hernia repair (liver, pancreas, or kidney) are 30.5cm x 35.6cm and 25.4cm x 33cm.

The limitations of this study include the fact that it was a retrospective case review study. Due to this study design, postoperative nursing care and data entry was not standardized for all patients. In addition, study blinding and randomization were not possible, resulting in possible bias. The study sample was modest, and the study may not have been adequately powered to reliably detect our secondary endpoints. We were also unable to detect the failure rate of either the epidural or the TAP catheters, since these data were not available in our electronic medical record.

Conclusions

Thoracic epidural catheter placement in transplant patients undergoing herniorraphy was introduced at Indiana University Hospital in order to improve post-operative analgesia. For these patients, postoperative pain control has historically been limited to intravenous and oral opioids. However, the use of opioids is associated with systemic opioid-related side effects, such as ileus and respiratory depression. These side effects put patients at risk for suboptimal pain control and an increased length of hospital stay. Using elastomeric pain pump devices for analgesia after hernia repair has not been shown to significantly decrease pain, opioid consumption, or length of hospital stay.[18] Epidural analgesia has been shown to provide good postoperative pain relief both after open liver resection and live liver donation.[19, 20] The use of epidural analgesia for post-operative pain control has also been found to reduce total opioid consumption. Our results expand upon these studies, showing the effectiveness of epidural analgesia in post-transplant populations. Our findings show that epidural analgesia was superior to continuous TAP block analgesia as well as analgesia with oral and parenteral medications. Epidural analgesia decreased post-operative pain scores and opioid usage for this group of patients.

We did not see a statistically significant difference in opioid-related side effects including ileus, aspiration, or respiratory depression between the three groups. We had hypothesized that the opioid-sparing effect of epidural analgesia would lead to a reduction in opioid-related side effects, but we did not observe this finding. The size and design of the study may have been suboptimal for detecting these secondary endpoints.

Although our number of patients in this study was small, we detected no infections related to the epidural or TAP block catheters in any of these immunosuppressed patients. Thus, our data support the usage of epidurals in immunosuppressed patients after organ transplant surgery. With the current opioid epidemics being declared a public health emergency, and the national movement towards decreasing opioid usage, our data further support the use of epidurals in this patient population.

References

[1] Smith, C. T., Katz, M. G., Foley, D., Welch, B., Leverson, G. E., Funk, L. M., & Greenberg, J. A. Incidence and risk factors of incisional hernia formation following abdominal organ transplantation. *Surg Endosc*. 2014;29(2):398-404. doi: 10.1007/s00464-014-3682-8.

[2] Tsirline, V. B., Colavita, P. D., Belyansky, I., Zemlyak, A. Y., Lincourt, A. E., & Heniford, B. T. Preoperative pain is the strongest predictor of postoperative pain and diminished quality of life after ventral hernia repair. *Am Surg*. 2013;79(8):829-836.

[3] Pham, C. T., Perera, C. L., Watkin, D. S., & Maddern, G. J. Laparoscopic ventral hernia repair: a systematic review. *Surg Endosc*. 2009;23(1):4-15. doi: 10.1007/s00464-008-0182-8.

[4] Nishikawa K, Kimura S, Shimodate Y, Igarashi M, Namiki A: A comparison of intravenous-based and epidural-based techniques for anesthesia and postoperative analgesia in elderly patients undergoing laparoscopic cholecystectomy. J Anesth 2007; 21:1–6Nishikawa, K Kimura, S Shimodate, Y Igarashi, M Namiki, A

[5] Flisberg, P., Rudin, Å., Linnér, R. and Lundberg, C. J. F. (2003), Pain relief and safety after major surgery A prospective study of epidural and intravenous analgesia in 2696 patients. Acta Anaesthesiologica Scandinavica, 47: 457–465. doi:10.1034/j.1399-6576.2003.00104.x

[6] Ballantyne JC, Carr DB, DeFerranti S et al. The comparative effects of postoperative analgesic therapies on pulmonary outcome: cumulative meta-analyses of randomised, controlled trials. Anesth Analg 1998: 86: 598–612.

[7] Saber, A. A., Elgamal, M. H., Rao, A. J., Itawi, E. A., & Martinez, R. L. Early experience with lidocaine patch for postoperative pain control after laparoscopic ventral hernia repair. Int J Surg. 2009;7(1):36-38. doi: 10.1016/j.ijsu.2008.09.003.

[8] McGuire, L., Heffner, K., Glaser, R. et al. Pain and wound healing in surgical patients. ann. behav. med. (2006) 31: 165.

[9] Morrison RS, Magaziner J, McLaughlin MA, et al.: The impact of post-operative pain on outcomes following hip fracture.Pain. 2003103:303–311.

[10] Block BM, Liu SS, Rowlingson AJ, Cowan AR, Cowan JA Jr, Wu CL. Efficacy of postoperative epidural analgesia: a meta- analysis. JAMA. 2003;290:2455–63

[11] Wu CL, Cohen SR, Richman JM, Rowlingson AJ, Courpas GE, Cheung K, Lin EE, Liu SS. Efficacy of postoperative patient-controlled and continuous infusion epidural analgesia versus intravenous patient-controlled analgesia with opioids: a meta-analysis. Anesthesiology. 2005;103:1079–88

[12] Park WY, Thompson JS, Lee KK and the Department of Veterans Affairs Cooperative Study #345 Study Group. Effect of epidural anesthesia and analgesia on perioperative outcome. A randomised, controlled veterans affairs cooperative study. Ann Surg 2001: 234: 560–71.

[13] Rigg JR, Jamrozik K, Myles PS et al. Epidural anaesthesia and analgesia and outcome of major surgery: a randomised trial. Lancet 2002: 359: 1276–82.

[14] Horlocker T. Complications of spinal and epidural anesthesia. Anesthesiol Clin North America. 2000;18:461–85.

[15] Gronwald, C., Vowinkel, T., & Hahnenkamp, K. Regional anesthetic procedures in immunosuppressed patients: risk of infection. *Curr Opin Anaesthesiol*. 2011;24(6):698-704. doi: 10.1097/ACO.0b013e32834cd2f0.

[16] Hebl, J. R., & Niesen, A. D. Infectious complications of regional anesthesia. *Curr Opin Anaesthesiol*. 2011;24(5):573-580. doi: 10.1097/ACO.0b013e32834a9252.

[17] Wang L, Hauerberg J, Schmidt J. Incidence of spinal epidural abscesses after epidural analgesia. Anesthesiology. 1999;91:1928–36.

[18] Rosen, M. J., Duperier, T., Marks, J., Onders, R., Hardacre, J., Ponsky, J., . . . Laughinghouse, M. Prospective randomized double-blind placebo-controlled trial of postoperative elastomeric pain pump devices used after laparoscopic ventral hernia repair. *Surg Endosc*. 2009;23(12):2637-2643. doi: 10.1007/s00464-009-0470-y.

[19] Schreiber, K. L., Chelly, J. E., Lang, R. S., Abuelkasem, E., Geller, D. A., Marsh, J. W., Tsung, A., Sakai, T. Epidural versus paravertebral nerve block for postoperative analgesia in patients undergoing open liver resection: a randomized clinical trial. *Reg Anesth Pain Med*. 2016;41(4):460-468. doi: 10.1097/AAP.0000000000000422.

[20] Clarke, H., Chandy, T., Srinivas, C., Ladak, S., Okubo, N., Mitsakakis, N., Holtzman, S., Grant, D., McCluskey, S. A., Katz, J. Epidural analgesia provides better pain management after live liver donation: a retrospective study. *Liver Transpl*. 2011;17(3):315-323. doi: 10.1002/lt.22221.

Table 1. ***Summary Statistics of Patient Demographics***

Variables	*Total N=154(%)*	*No Intervention N=47(%)*	*Epidural N=56(%)*	*TAP Catheter N=51(%)*	*P Value*
Age on day of surgery					*0.077* [A]
Mean ± SE	54.3 ± 0.813	55.4 ± 1.32	55.8 ± 1.51	51.8 ± 1.30	
Median (min - max)	55 (26 - 81)	57 (30 - 78)	55.5 (26 - 81)	53 (32 - 77)	
Gender					*0.116* [C]
Male	103 (67)	37 (79)	35 (63)	31 (61)	
Female	51 (33)	10 (21)	21 (37)	20 (39)	
BMI					*0.449* [A]
Mean ± SE	30.6 ± 1.3	31.1 ± 0.8	32.2 ± 3.4	28.4 ± 0.7	
Median (min - max)	28.6 (17.6 - 215.0)	29.9 (20.9 - 47.1)	28.2 (17.6 - 215.0)	28.0 (19.2 - 43.5)	
Type of Previous Transplant					*0.002* [C] [+]
Liver	83 (54)	36 (77)	30 (53)	17 (33)	
Kidney	14 (9)	2 (4)	4 (7)	8 (16)	
Pancreas	25 (16)	2 (4)	11 (20)	12 (24)	
Pancreas/Kidney	32 (21)	7 (15)	11 (20)	14 (27)	
Duration of Surgery (minute)					*0.002* [A]
Mean ± SE	226 ± 6.43	258 ± 14.5	220 ± 7.39	204 ± 10.4	
Median (min - max)	209.5 (40 - 471)	250 (52 - 440)	209 (104 - 408)	199 (40 - 471)	
Blood_loss (ml)					*<.001* [A]
Mean ± SE	47.9 ± 6.0	83.4 ± 16.0	22.3 ± 3.1	43.3 ± 7.9	
Median (min - max)	20.0 (3.0 - 600.0)	50.0 (10.0 - 600.0)	10.0 (3.0 - 100.0)	20.0 (5.0 - 300.0)	
Type_of_hernia					*0.103* [C]
Open	17 (11)	9 (19)	4 (7)	4 (8)	
Laparoscopic	137 (89)	38 (81)	52 (93)	47 (92)	

[+]Exact test
[A]ANOVA F-test; [C]Chi-square test; [K]Kruskal-Wallis test

Table 2. Pain score and Opioid usage comparison for day1

Variables	*Total N=154(%)*	*No Intervention N=47(%)*	*Epidural N=56(%)*	*TAP Catheter N=51(%)*	*P Value*
Median_pain					*0.100* [A]
Mean ± SE	4.4 ± 0.2	4.8 ± 0.3	3.9 ± 0.3	4.7 ± 0.3	
Median (min - max)	5.0 (0.0 - 10.0)	4.5 (1.0 - 10.0)	4.5 (0.0 - 9.0)	5.0 (0.0 - 8.0)	
Mean_pain					*0.044* [A]
Mean ± SE	4.5 ± 0.2	4.8 ± 0.3	3.9 ± 0.3	4.8 ± 0.2	
Median (min - max)	4.6 (0.0 - 9.5)	4.7 (1.1 - 9.5)	4.1 (0.0 - 8.0)	5.0 (0.9 - 8.0)	
Max_pain					*0.009* [A]
Mean ± SE	6.5 ± 0.2	7.0 ± 0.3	5.7 ± 0.3	6.9 ± 0.3	
Median (min - max)	7.0 (0.0 - 10.0)	7.0 (2.0 - 10.0)	6.0 (0.0 - 10.0)	7.0 (3.0 - 10.0)	
Ivmorphine					*<.001* [A]
Mean ± SE	4.6 ± 0.8	4.0 ± 1.0	1.1 ± 0.5	8.9 ± 2.0	
Median (min - max)	0.0 (0.0 - 56.7)	0.0 (0.0 - 32.5)	0.0 (0.0 - 19.5)	5.0 (0.0 - 56.7)	

[+]Exact test
[A]ANOVA F-test; [C]Chi-square test; [K]Kruskal-Wallis test

Table 3. Pain score and Opioid usage comparison for day2

Variables	*Total N=151(%)*	*No Intervention N=47(%)*	*Epidural N=55(%)*	*TAP Catheter N=49(%)*	*P Value*
Median_pain					*0.002* [A]
Mean ± SE	3.5 ± 0.2	3.9 ± 0.3	2.7 ± 0.3	4.0 ± 0.3	
Median (min - max)	4.0 (0.0 - 10.0)	4.0 (0.0 - 7.0)	3.0 (0.0 - 7.5)	4.0 (0.0 - 10.0)	
Mean_pain					*0.004* [A]
Mean ± SE	3.6 ± 0.2	4.0 ± 0.3	2.9 ± 0.3	4.0 ± 0.2	
Median (min - max)	3.8 (0.0 - 8.8)	4.1 (0.0 - 7.4)	2.6 (0.0 - 7.5)	4.1 (0.5 - 8.8)	
Max_pain					*0.013* [A]
Mean ± SE	5.5 ± 0.2	6.1 ± 0.3	4.7 ± 0.4	5.7 ± 0.3	
Median (min - max)	5.0 (0.0 - 10.0)	6.0 (0.0 - 10.0)	4.0 (0.0 - 10.0)	6.0 (1.0 - 10.0)	
Ivmorphine					*0.014* [A]
Mean ± SE	8.4 ± 1.8	8.3 ± 1.3	2.4 ± 0.9	15.2 ± 5.3	
Median (min - max)	2.5 (0.0 - 252.5)	8.0 (0.0 - 35.0)	0.0 (0.0 - 36.0)	6.0 (0.0 - 252.5)	

[+]Exact test
[A]ANOVA F-test; [C]Chi-square test; [K]Kruskal-Wallis test

Table 4. Pain score and Opioid usage comparison for day3

Variables	*Total N=135(%)*	*No Intervention N=44(%)*	*Epidural N=51(%)*	*TAP Catheter N=40(%)*	*P Value*
Median_pain					*0.018* [A]
Mean ± SE	3.2 ± 0.2	3.7 ± 0.3	2.5 ± 0.3	3.6 ± 0.4	
Median (min - max)	3.0 (0.0 - 10.0)	4.0 (0.0 - 8.0)	2.0 (0.0 - 8.0)	3.5 (0.0 - 10.0)	
Mean_pain					*0.019* [A]
Mean ± SE	3.3 ± 0.2	3.6 ± 0.3	2.6 ± 0.3	3.7 ± 0.3	
Median (min - max)	3.4 (0.0 - 9.5)	3.8 (0.0 - 7.7)	2.4 (0.0 - 7.4)	3.8 (0.0 - 9.5)	
Max_pain					*0.046* [A]
Mean ± SE	5.0 ± 0.2	5.5 ± 0.3	4.3 ± 0.4	5.4 ± 0.4	
Median (min - max)	5.0 (0.0 - 10.0)	5.0 (0.0 - 9.0)	4.0 (0.0 - 10.0)	5.0 (0.0 - 10.0)	
Ivmorphine					*0.084* [A]
Mean ± SE	12.7 ± 4.5	9.0 ± 1.8	4.2 ± 0.9	27.7 ± 14.7	
Median (min - max)	3.3 (0.0 - 585.0)	5.5 (0.0 - 65.0)	0.0 (0.0 - 30.0)	5.8 (0.0 - 585.0)	

[+]Exact test
[A]ANOVA F-test; [C]Chi-square test; [K]Kruskal-Wallis test

Table 5. Adverse Reaction Comparisons Between Two Groups

Variables	*Total N=154(%)*	*No epidural N=98(%)*	*Epidural N=56(%)*	*P Value*
Nausea (Promethazine, Ondansetron, etc)				*0.215*
NO	131 (85)	86 (88)	45 (80)	
YES	23 (15)	12 (12)	11 (20)	
Vomit				*1.000*
NO	150 (97)	95 (97)	55 (98)	
YES	4 (3)	3 (3)	1 (2)	
Respiratory Depression				
NO	154 (100)	98 (100)	56 (100)	
Naloxone given				*0.364*
NO	153 (99)	98 (100)	55 (98)	
YES	1 (1)	0 (0)	1 (2)	
Pneumonia				*0.364*
NO	153 (99)	98 (100)	55 (98)	
YES	1 (1)	0 (0)	1 (2)	
Aspiration				*0.184*
NO	154 (100)	98 (100)	56 (100)	

Table 6. Other outcome variable comparisons between three groups

Variables	*Total N=154(%)*	*No Intervention N=47(%)*	*Epidural N=56(%)*	*TAP Catheter N=51(%)*	*P Value*
Time TO first flatus					*0.104* [A]
Mean ± SE	61.1 ± 2.36	68.3 ± 4.41	56.0 ± 3.72	60.5 ± 4.10	
Median (min - max)	59.9 (2.12 - 148.2)	70.2 (8.28 - 148.1)	55.6 (2.12 - 105.3)	58.6 (17.2 - 127.4)	
Time TO first BM					*0.416* [A]
Mean ± SE	80.7 ± 2.6	86.0 ± 4.6	78.8 ± 3.2	78.0 ± 5.77	
Median (min - max)	77.1 (6.3 - 271.7)	83.9 (6. 3 - 190.4)	78.4 (39.6 - 137.7)	67.6 (39.3 - 271.7)	
Length of hospital stay:					*0.152* [A]
Mean ± SE	7.54 ± 0.78	8.64 ± 2.05	8.58 ± 1.24	5.40 ± 0.39	
Median (min - max)	5.31 (2.1 - 98.2)	5.81 (3.0 - 98.2)	6.19 (2.9 - 52.4)	4.25 (2.1 - 14.3)	

[+]Exact test
[A]ANOVA F-test; [C]Chi-square test; [K]Kruskal-Wallis test